Response to 'Correspondence on 'Impact of rheumatoid arthritis on major cardiovascular events in patients with and without coronary artery disease" by Jong *et al*

We appreciate the interest and comments by Jong *et al*[1] concerning our study: 'Impact of rheumatoid arthritis on major cardiovascular events in patients with and without coronary artery disease'.[2] We would like to clarify and discuss the issues raised by Jong *et al*.[1] The comments by our colleagues highlight many inherent limitations of an epidemiological study that may provide considerations for a future prospective randomised trial.

First, Jong *et al*[1] note that that low-density lipoprotein cholesterol (LDL-C) level was not part of the baseline characteristics. The reason is that biochemical data are currently not available from the national Danish Registries. While we do agree with our colleagues that LDL-C is a player in the pathogenesis of coronary artery disease (CAD) and that LDL-C is an independent predictor of cardiovascular events, there are several more important factors that were included. These are age, gender, heart failure, hypertension, diabetes, smoking and most importantly, the presence or absence of CAD.[3–5] Further, most of those with CAD were subsequently treated with statins, which reduces the baseline LDL-C levels and modifies the influence of this baseline characteristic.[6] We used statin treatment as a proxy for hypercholesterolaemia in the adjusted multivariate regression analysis.

Second, Jong *et al*[1] raise an interesting question regarding the impact of high-intensity versus low-intensity statins. Simvastatin was the primary statin used among all patients with rheumatoid arthritis (RA) in this study (44%, median dose 40 mg/daily), followed by high-intensity statins, atorvastatin (19%, median dose 40 mg/daily) and rosuvastatin (3%, median dose 10 mg/daily). It remains an open question whether early initiation of statin treatment will affect long-term outcomes in patients with RA and no CAD, and whether high-intensity versus low-intensity statin treatment will make a difference.[7] In the presence of CAD, however, statin treatment will aim to reach the levels dictated by the guidelines issued by scientific societies.

Third, Jong *et al*[1] speculate that treatment compliance rates for patients with RA may have been suboptimal. However, the baseline medical treatment, based on prescription dispensations, did not show any significant differences in filling of prescriptions of aspirin, ADP-inhibitor and statins.[2]

The fourth and final comment address that our study was based on a coronary angiography cohort. We agree, as also stated in our original publications,[2 8–10] that this is a potential limitation. Since we aimed to assess the impact of CAD on long-term future events, we needed to look at patients who had undergone coronary angiography. This may have introduced selection bias, since patients with RA are more likely to be referred to coronary angiography. However, compared with the general population, patients with no CAD by coronary angiography have a lower risk of myocardial infarction and similar mortality.[11] Propensity score matching is one way of adjusting for potential baseline differences but it is only prospective randomised clinical trials that has the potential to remove unmeasured confounding.

Brian Bridal Løgstrup ,[1] **Kevin Kris Warnakula Olesen** ,[1] **Dzenan Masic**,[2] **Christine Gyldenkerne**,[1] **Pernille Gro Thrane**,[1] **Torkell Ellingsen** ,[3] **Hans Erik Bøtker**,[1] **Michael Maeng**[1]

[1]Department of Cardiology, Aarhus University Hospital Skejby, Aarhus, Denmark
[2]Department of Rheumatology, Silkeborg Regional Hospital, Silkeborg, Denmark
[3]Rheumatology, Odense University Hospital, Odense, Denmark

Correspondence to Dr Brian Bridal Løgstrup, Department of Cardiology, Aarhus University Hospital Skejby, Aarhus 8200, Denmark; bbl@dadlnet.dk

Handling editor Josef S Smolen

Contributors All coauthors have contributed equal to this answer to correspondence. All authors have approved the final draft.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not required.

Provenance and peer review Commissioned; internally peer reviewed.

© Author(s) (or their employer(s)) 2023. No commercial re-use. See rights and permissions. Published by BMJ.

Check for updates

To cite Løgstrup BB, Olesen KKW, Masic D, *et al*. *Ann Rheum Dis* 2023;**82**:e12.

Received 13 October 2020
Accepted 14 October 2020
Published Online First 2 November 2020

Linked

► http://dx.doi.org/10.1136/annrheumdis-2020-219201

Ann Rheum Dis 2023;**82**:e12. doi:10.1136/annrheumdis-2020-219231

ORCID iDs
Brian Bridal Løgstrup http://orcid.org/0000-0002-4218-0033
Kevin Kris Warnakula Olesen http://orcid.org/0000-0002-0560-3615
Torkell Ellingsen http://orcid.org/0000-0003-0426-4962

REFERENCES

1 Jong GP, Pan LF, Lin TK. Correspondance on "Impact of rheumatoid arthritis on major cardiovascular events in patients with and withoyt coronary artery disease". *Ann Rheum Dis* 2023;82:e11.
2 Løgstrup BB, Olesen KKW, Masic D, *et al*. Impact of rheumatoid arthritis on major cardiovascular events in patients with and without coronary artery disease. *Ann Rheum Dis* 2020;79:1182–8.
3 Steensig K, Olesen KKW, Madsen M, *et al*. A novel model for prediction of thromboembolic and cardiovascular events in patients without atrial fibrillation. *Am J Cardiol* 2020;131:40–8.
4 Løgstrup BB, Ellingsen T, Pedersen AB, *et al*. Development of heart failure in patients with rheumatoid arthritis: a Danish population-based study. *Eur J Clin Invest* 2018;48:e12915–8.
5 Løgstrup BB, Ellingsen T, Pedersen AB, *et al*. Heart failure and ischemic heart disease in patients with rheumatoid arthritis. *J Am Coll Cardiol* 2017;70:3069–71.
6 Svensson E, Nielsen RB, Hasvold P, *et al*. Statin prescription patterns, adherence, and attainment of cholesterol treatment goals in routine clinical care: a Danish population-based study. *Clin Epidemiol* 2015;7:213–23.
7 Svensson AL, Christensen R, Persson F, *et al*. Multifactorial intervention to prevent cardiovascular disease in patients with early rheumatoid arthritis: protocol for a multicentre randomised controlled trial. *BMJ Open* 2016;6:e009134.
8 Olesen KKW, Madsen M, Egholm G, *et al*. Patients with diabetes without significant angiographic coronary artery disease have the same risk of myocardial infarction as patients without diabetes in a real-world population receiving appropriate prophylactic treatment. *Diabetes Care* 2017;40:1103–10.
9 Olesen KKW, Madsen M, Gyldenkerne C, *et al*. Diabetes mellitus is associated with increased risk of ischemic stroke in patients with and without coronary artery disease. *Stroke* 2019;50:3347–54.
10 Gyldenkerne C, Olesen KKW, Madsen M, *et al*. Association between anti-diabetes treatments and cardiovascular risk in diabetes patients with and without coronary artery disease. *Diab Vasc Dis Res* 2019;16:351–9.
11 Olesen KK, Madsen M, Würtz M, *et al*. Risk of myocardial infarction in patients without angiographic coronary artery disease compared with the general population. *Am J Cardiol* 2020;132:8–14.

Ann Rheum Dis: first published as 10.1136/annrheumdis-2020-219231 on 2 November 2020. Downloaded from http://ard.bmj.com/ on April 17, 2024 by guest. Protected by copyright.